Los Alamos and Malaysian University collaborate to find genetic markers for dwarfism

January 12, 2012

LOS ALAMOS, New Mexico, January 12, 2012—Los Alamos National Laboratory and the Centre for Chemical Biology at Universiti Sains Malaysia (CCB@USM) have launched a human genome project to study an individual with achondroplasia disorder, the most common form of dwarfism.

The project began with the dream of Malaysian graduate student Ling Sze Lee to answer the question "Why am I different?" Using unique methods for high-throughput sequencing of ultra-low quantity chromosomal DNA and advanced sequence analysis, the team and Lee herself hope to identify previously unknown genomic markers for this disease to better understand its cause and to aid in the development of therapeutics and/or methods of prevention. The LANL Genome Science Group has already

completed the sequencing of all 23 chromosomes of the study's volunteer patient, a graduate student at the Universiti Sains Malaysia.

Achondroplasia is the most common cause of short-limbed dwarfism in humans, with the term achondroplasia meaning "without cartilage formation." In fact, cartilage is formed, but the development of long bones fails to occur completely. This genetic disease has social and medical complications including delayed motor milestones, leg bowing, lower back pain, respiratory complications such as apnea, middle ear disease, speech delay and articulation problems, obesity, and dental crowding. Sequencing the genomes of people with achondroplasia provides clues to diagnosis, treatment, and prevention of this and other genetic diseases.

Prior to this work, a tiny mutation in a growth factor gene (fgfr3), located in chromosome 4, had been identified as the cause of achondroplasia. In an effort to learn more about her own dwarfism, graduate student Lee volunteered to have her genome sequenced.

Lee optimized the isolation of the individual chromosomes from her own blood sample using flow cytometry, and the initial sequence analysis of Lee's chromosome 4 indicated that the classical diagnostic mutations of achondroplasia and hypochondroplasia were absent.

This result shows that gene fgfr3 is not the only marker for achondroplasia. To identify other possible markers, the remaining 22 chromosomes have been isolated and sequenced. Lee plans to come to Los Alamos in February to spend approximately a month working directly with the Genome Science Group to analyze the genome data. Her hope is that they can identify the alternate cause of her dwarfism—leading to a better understanding of the genetics of the disorder.

Los Alamos National Laboratory and Universiti Sains Malaysia signed a Memorandum of Understanding in September solidifying their joint interest for the application of scientific research and technology development to help tackle this crippling disorder. Funding is from the Malaysia Ministry of Higher Education under an Accelerated Program for Excellence grant.